Review article

Central liponeurocytoma as a clinical entity

Ali Börekci a, Pınar Kuru Bektaşoğlu a,b,*, Ali Fatih Ramazanoğlu c, Bora Gürer a, Erhan Çelikoğlu a

aTurkish Ministry of Health, University of Health Sciences, Fatih Sultan Mehmet Education and Research Hospital, Department of Neurosurgery, Istanbul, Turkey
bMarmara University School of Medicine, Department of Physiology, Istanbul, Turkey
cTurkish Ministry of Health, University of Health Sciences, Umraniye Education and Research Hospital, Department of Neurosurgery, Istanbul, Turkey

ARTICLE INFO

Article history:
Received 25 February 2018
Accepted 1 September 2018
Available online 11 September 2018

Keywords:
Liponeurocytoma
Lateral ventricle
Supratentorial

ABSTRACT

Introduction: Liponeurocytomas are mostly localized in cerebellar hemispheres and the second most common location is the vermis. It is rarely observed within the intracranial ventricles. Here, we present a case of liponeurocytoma located in the right lateral ventricle and the systematic review of the literature.

State of the art: We searched PubMed with keyword ‘central liponeurocytoma’ and the references of the related articles. There were no language or year restrictions. We included articles focusing on liponeurocytomas located in the central nervous system leaving a total of 17 articles and 21 reported cases.

Clinical implications: A 62-year-old female presented with confusion and mental disorientation without any other neurological deficit. Her magnetic resonance imaging (MRI) revealed a lateral ventricle located mass lesion which was hypointense on T1-weighted images (WI) and heterogeneously hyperintense on T2-WI with cystic component. Via craniotomy, yellow-beige colored, soft and moderately vascularized mass lesion was gross totally resected. Despite postoperative MRI revealed total resection, patient had left-sided hemiparesis. The patient recovered well in her postoperative period and there was no recurrence on her 6th month follow-up MRI.

Future directions: Intraventricular liponeurocytoma has a favorable clinical course, and radiological features may be useful in the diagnosis of this rare tumor before surgery. Supratentorial intraventricular location should be kept in mind in the differential diagnosis of the lateral ventricular tumors.

© 2018 Polish Neurological Society. Published by Elsevier Sp. z o.o. All rights reserved.
1. Introduction

The cerebellar liponeurocytoma is a rare, well-differentiated neuronal and variable astrocytic tumor of the central nervous system (CNS) that arises in adults and typically shows focal or regional lipomatous differentiation [1]. Liponeurocytomas are predominantly localized in cerebellar hemispheres and the second most common location is the vermis. It is occasionally located in supratentorial lateral ventricle and the fourth ventricle [2,3]. To the best of our knowledge, 47 cases in the cerebellum, 15 cases in the lateral ventricle, 2 cases in the 3rd ventricle and 2 cases in the 4th ventricle had been reported [3–5]. Due to the limited number of cases, little is known about the supratentorial intraventricular liponeurocytoma when compared to the cerebellar form [3]. Because of its rarity and lack of long-term follow-up data, the biological behaviors and clinical features of this tumor are still not well understood. In recent years, it is indicated that patients with cerebellar liponeurocytomas usually show a desirable clinical course after neurosurgical removal, which means that the correct diagnosis is very important in order to avoid unnecessary adjuvant therapy. Here, we present a 62-year-old woman with right lateral ventricular liponeurocytoma with a detailed review of literature of liponeurocytomas located in supratentorial areas.

1.1. Literature search

We searched PubMed with keyword ‘central liponeurocytoma’ and the references of the related articles. There were no language or year restrictions. We included articles focusing on liponeurocytomas located in the CNS, leaving a total of 17 articles and 21 reported cases. The PRISMA flowchart for the elimination of the articles is shown in the Supplementary Checklist.

1.2. Case description

A 62-year-old female patient presented with confusion and mental disorientation without any other neurological deficits. In her previous medical history, she had bilateral adrenalectomy, diagnosed as Cushing disease 22 years ago, under medication, operated 1 year ago for colon cancer, and took chemotherapy. There was no active comorbidities or evidence of organ failure at the time of the surgery. Magnetic resonance imaging (MRI) revealed a lobulated mass lesion located at the right lateral ventricle also expanding through the left side of the midline. Lesion was hypointense on T1-WI and heterogeneously hyperintense on T2-WI with cystic component. On T1-WI, hemorrhagic component was seen at the lateral part of the lesion. There was heterogeneous contrast enhancement at the central part (Fig. 1). The patient underwent interhemispheric transcicallosal approach via right-sided craniotomy for microsurgical resection of the lesion. The lesion was yellow-beige colored, soft suckable and moderately vascularized. Gross total resection was achieved. Despite postoperative MRI revealed total resection, patient had left-sided hemiparesis. It is thought that postoperative hemiparesis is possibly caused by interhemispheric retraction. Hemiparesis was resolved with the aid of physiotherapy gradually within 6 months. The patient recovered well in her postoperative period, and there was no recurrence on her 6th month follow-up MRI. The pathological diagnosis was liponeurocytoma WHO grade II. Histopathological examination of the tumor tissue revealed no nuclear atypia, no mitosis, no hypercellularity and no necrosis. Round or oval nucleus, thin
chromatin, mostly clear cytoplasmic diffuse proliferation were observed (Fig. 2). Single or multiple adipocyte like lipidized cells were observed (200× magnification). Immunohistochemical evaluation was positive for early and mature neuronal markers such as glial fibrillary acidic protein (GFAP), synaptophysin and neuron-specific enolase (NSE). Epithelial membrane antigen (EMA), cromogranin A and P53 were negative. In our case, she had multiple systemic diseases and died 1 year after surgery due to multiple organ dysfunctions. Case reports and review articles are exempt from ethical committee approval in our institution. The informed consent is obtained from patient and her family.

2. Discussion

Liponeurocytomas are rare benign CNS neoplasms with a favorable clinical prognosis [6]. The peak incidence is from 30 to 60 years old, and the mean age is approximately 53 years. Men and women are equally affected [7]. This tumor type has low proliferative potential, especially when compared to medulloblastoma, the primitive neuroectodermal tumor of the cerebellum from which the liponeurocytoma needs to be distinguished [8]. However, recurrence may occur and malignant progression had been reported. The tumor is mainly involved in cerebellar hemisphere, but can also be located in the paramedian region or vermis and extend to the cerebello-pontine angle or fourth ventricle [7]. Limiting the occurrence of liponeurocytoma unnecessarily to cerebellum obscures the presence of similar neoplasms at the other locations. Twenty-one intraventricular liponeurocytoma cases had been reported in the literature [2,3]. We herein present a 62-year-old woman, the 22nd example of intraventricular liponeurocytoma with a review of the literature. Detailed review of intraventricular liponeurocytoma cases were presented in Table 1.

The main clinical presentations such as headache and vomiting were usually related to increased intracranial pressure due to mass effect and hydrocephalus [3]. Our case presented with mental disorientation and confusion. On CT, the tumor is variably isodense or hypodense, with focal areas of marked hypoacluence corresponding to fat density [7,9]. On T1-WI, the tumor is isointense to hypointense, with patchy areas of hyperintensity corresponding to regions of high lipid

Figure 2 – (A) Photomicrograph of tumor tissue with hematoxylin and eosin stain showing round or oval nucleus, thin chromatin, mostly clear cytoplasmic diffuse proliferation (200× magnification). (B) Single or multiple adipocyte like lipidized cells were observed (200× magnification). Immunohistochemical evaluation was early and mature neuronal markers positive such as (C) GFAP (400× magnification), (D) synaptophysin (200× magnification) and (E) NSE (200× magnification). (F) There was no staining with P53 (200× magnification).
<table>
<thead>
<tr>
<th>Authors</th>
<th>Age/sex</th>
<th>Clinical features</th>
<th>Site</th>
<th>Imaging findings</th>
<th>Treatment</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horoupian et al., 1997</td>
<td>30 years/M</td>
<td>Headache for 3 months, nausea, vomiting, blurred vision during the past few weeks, bilateral grade III papilledema with 10/70 visual acuity and enlargement of blind spots</td>
<td>Left lateral ventricle, 3rd ventricle, corpus callosum</td>
<td>CT and MRI of the brain showed a 5.0 × 4.0 × 3.5 cm deep, nonhomogenous mass with mixed signals indicating the presence of fat and possibly calcium. The tumor filled the left lateral ventricle and extended rostrocaudally over the length of the body of the corpus callosum and roof of the 3rd ventricle encroaching into the periventricular white matter. Both lateral ventricles were dilated</td>
<td>Subtotal resection</td>
<td>Five months after surgery, the patient had mild weakness of dorsi- and plantar flexion of the right foot and moderate memory deficits and motor apraxia. His vision recovered almost fully on the left but partially on the right. He was subsequently lost to follow-up</td>
</tr>
<tr>
<td>George et al., 2001</td>
<td>59 years/F</td>
<td>-</td>
<td>Anterior horn, left lateral ventricle</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Rajesh et al., 2003</td>
<td>30 years/M</td>
<td>Headache, instability of gait for 3 months. Right-sided cerebellar signs and VI cranial nerve paresis</td>
<td>Frontal horn, lateral ventricle</td>
<td>MRI revealed a mass lesion measuring 7.8 × 6.7 × 6 cm in the body and frontal horn of the lateral ventricle. The lesion was infiltrating the corpus callosum</td>
<td>Near total excision</td>
<td>Postoperatively, the patient developed massive intraventricular bleeding on the third day and died</td>
</tr>
<tr>
<td>Kuchelmeister et al., 2006</td>
<td>35 years/M</td>
<td>Headache 3 years, amnesia, dizziness</td>
<td>Left lateral ventricle</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Aytac et al., 2009</td>
<td>55 years/F</td>
<td>Intermittent severe headache associated with blurring of vision and diplopia for 5 months, generalized weakness. Bilateral papilledema and bilateral 6th nerve palsy</td>
<td>Left lateral ventricle</td>
<td>MRI: iso-heterogeneous intensity on T1-WI and hyperintense on T2-WI MRI brain scan revealed an inhomogeneously enhancing large intraventricular mass filling the body and lateral horn of right ventricle The mass measured 5 × 3 × 1 cm and showed areas of calcification</td>
<td>Gross total resection</td>
<td>Patient required a ventriculoperitoneal shunt on the 10th post-operative day. His subsequent recovery was satisfactory and at the time of discharge his Glasgow coma scale score was 14</td>
</tr>
<tr>
<td>Pankaj et al., 2010</td>
<td>35 years/M</td>
<td>Bifrontal headache: 4 months, blurring of vision: 15 days. Bilateral papilledema</td>
<td>Bilateral lateral ventricle</td>
<td>CT: mixed density, irregular mass lesion, bilateral lateral ventricles causing hydrocephalus. Third and 4th ventricles normal</td>
<td>Radical excision</td>
<td>Recurrence 9 years and 4 months later. Re-exploration and radical excision of the tumor performed with postoperative radiotherapy. No recurrence at 2-year follow-up</td>
</tr>
<tr>
<td>Chakraborti et al., 2011</td>
<td>36 years/M</td>
<td>Intermittent, holocranial headache and vomiting for 2 years. Bilateral papilledema</td>
<td>Lateral and 3rd ventricle</td>
<td>CT: irregular, hypodense lesion occupying both the lateral and 3rd ventricles. MRI: lesion was hyperintense on T1-WI and T2-WI images with specks of hypointensity</td>
<td>Gross total resection</td>
<td>Post-operative period was uneventful and the patient was lost for follow-up</td>
</tr>
<tr>
<td></td>
<td>30 years/M</td>
<td>Intermittent, holocranial headache, left lower limb weakness for 6 months. Bilateral papilledema</td>
<td>Bilateral lateral ventricle, central</td>
<td>CT: hyperdense, irregular, lobulated, minimally enhancing mass lesion, in the septal area extending into both lateral ventricles, asymmetrically causing hydrocephalus</td>
<td>Gross total excision</td>
<td>Post-operative period was uneventful and the patient was lost for follow-up</td>
</tr>
<tr>
<td>Authors</td>
<td>Age/sex</td>
<td>Clinical features</td>
<td>Site</td>
<td>Imaging findings</td>
<td>Treatment</td>
<td>Prognosis</td>
</tr>
<tr>
<td>-------------------------</td>
<td>---------------</td>
<td>----------------------------------------------------</td>
<td>---------------------------</td>
<td>-------------------------------------------------------------------------------------------------------</td>
<td>----------------------</td>
<td>---------------------------------------------------------------------------</td>
</tr>
<tr>
<td>den Hollander et al., 2011 [31]</td>
<td>43 years/M</td>
<td>—</td>
<td>Right lateral ventricle</td>
<td>—</td>
<td>Gross total resection</td>
<td>Not specified</td>
</tr>
<tr>
<td>Gupta et al., 2011 [23]</td>
<td>45 years/M</td>
<td>—</td>
<td>Trigone of lateral ventricle</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Ding et al., 2014 [32]</td>
<td>52 years/F</td>
<td>Headache for 10 days</td>
<td>Third ventricle</td>
<td>CT: round hypodense lesion with dark area suggestive of fatty tissue, and also speckled calcification</td>
<td>Gross total resection</td>
<td>No recurrence at 10 months, and the patient was lost for follow-up</td>
</tr>
<tr>
<td>Karabagli et al., 2014 [2]</td>
<td>34 years/M</td>
<td>Headache</td>
<td>Third ventricle</td>
<td>On T1-WI showed a large, partly cystic, 4 x 5 cm mass in the 3rd ventricle with heterogeneous enhancement with gadolinium</td>
<td>Gross total resection</td>
<td>No recurrence at 2 years</td>
</tr>
<tr>
<td>Ruiz Ginés et al., 2014 [33]</td>
<td>33 years/M</td>
<td>Cural sensitive symptoms, recent onset headache</td>
<td>Supratentorial, tumor</td>
<td>Intraventricular, multicystic, heterogeneous and with areas of associated lipomatosis</td>
<td>Gross total resection</td>
<td>Not specified</td>
</tr>
<tr>
<td>Wang et al., 2016 [34]</td>
<td>30 years/M</td>
<td>Headache dizziness for 1 months</td>
<td>Right lateral ventricle</td>
<td>CT: slightly hypodense round lesion with small cystic areas</td>
<td>Gross total resection</td>
<td>Not mentioned</td>
</tr>
<tr>
<td>Xu et al., 2017 [3]</td>
<td>29 years/M</td>
<td>Headache for 3 months, vomiting</td>
<td>Right lateral ventricle</td>
<td>CT: an isodense to slight hyperdense round mass; MRI: heterogeneous intensity on T1-WI and T2-WI</td>
<td>Gross total resection</td>
<td>No recurrence at 2 years</td>
</tr>
<tr>
<td></td>
<td>48 years/F</td>
<td>Headache for 12 months, numbness</td>
<td>Forth ventricle</td>
<td>MRI: an irregular mass with isointensity on T1 and T2-WI, several microcysts and slight enhancement on contrast</td>
<td>Gross total resection</td>
<td>No recurrence at 5 years</td>
</tr>
<tr>
<td>Shi et al., [3]</td>
<td>36 years/M</td>
<td>Headache dizziness for 12 months</td>
<td>Left lateral ventricle</td>
<td>CT: hypo-to isodense mass lesion. MRI: isointense on T1-WI and T2-WI, short T1 hyperintense displayed on T1-WI</td>
<td>Gross total resection</td>
<td>No recurrence at 2.5 years, and the patient was lost for follow-up</td>
</tr>
<tr>
<td>Xu et al., 2017 [35]</td>
<td>29 years/M</td>
<td>Right lateral ventricle</td>
<td>Headache (1 month). Physical and neurological examinations unremarkable</td>
<td>MRI: a well-demarcated solid lesion with multiple small cysts and moderate heterogeneous enhancement No perilesional edema</td>
<td>Gross total resection</td>
<td>No recurrence at 1 year and 5 months</td>
</tr>
<tr>
<td>Cai et al., 2018 [36]</td>
<td>11 years/M</td>
<td>Intermittent headache, nausea and vomiting</td>
<td>Right cerebral hemisphere</td>
<td>CT: An irregular hypodense and isodense mixed mass in the right frontal lobe MRI: A large cystic—solid mass approximately 4.5 x 4.7 x 6.4 cm in size, in the right frontal lobe. The solid part of the mass exhibited heterogeneous isointensity on T1-WI and T2-WI</td>
<td>Gross total resection</td>
<td>No clinical or neuroradiological evidence of recurrence or residual of the tumor was found 6 years and 2 months after initial surgery</td>
</tr>
</tbody>
</table>

CT, computed tomography; FLAIR, fluid attenuated inversion recovery; FSE, fast spin echo; MRI, magnetic resonance imaging; WI, weighted imaging.
content. It must be kept in mind that all liponeurocytomas may not reveal this hyperintensity on T1-WI because of different content of fat tissue within the tumor. The hyperintensity on T1-WI reflecting fat within the tumor can be suppressed to hypointensity in fat-suppression sequence. This signal intensity change may be useful in determining a preoperative diagnosis of liponeurocytoma [9]. MRI findings of the tumor of our case were hypointense on T1-WI, and hemorrhagic component was seen at the lateral part of the lesion. Enhancement with gadolinium is usually heterogeneous, with areas of tumor showing variable degrees of enhancement implying mild vascularity in intraventricular liponeurocytomas. In addition, several microcysts were also clearly displayed on T1- and T2-WI. There was heterogeneous contrast enhancement at the central part in our case. On T2-WI, the tumor is slightly hyperintense to the adjacent brain, with focal areas of marked hyperintensity. Our case was also heterogeneously hyperintense on T2-WI with cystic component. Associated edema is usually minimal or absent [10]. On diffusion-weighted images, the non-fat component of the tumors revealed mildly restricted diffusion, which reflected the histopathological features of the tumors such as small tumor cells, less cytoplasm and closely arranged tissue cells.

Cerebellar liponeurocytomas have been included in the 2000 World Health Organization (WHO) classification of tumors of the CNS, under the heading of glioneuronal tumors, grade I neoplasm; the 2007 WHO classification assigns cerebellar liponeurocytoma to WHO grade II in light of low proliferation but high likelihood of tumor recurrences [6,11,12]. In 2016 WHO classification, cerebellar liponeurocytoma was also accepted as grade II histopathologically recurrences [6]. As many as 50–60% of these tumors will recur within periods ranging from 1 to 12 years [6,13,14]. The time to clinical progression is often long (mean: 6.5 years), but in some cases relapse occurs within a few months [15]. There are no accepted histologic features of liponeurocytoma that can distinguish tumors according to recurrence risk.

In histological examination, isomorphic small neurocytic cells arranged in sheets and lobules and with regular round to oval nuclei, clear cytoplasm and poorly defined cell membranes. Focal lipomatous differentiation could also be seen [3]. The histological hallmark of this entity is focal accumulation of lipid-laden cells that resemble adipocytes but constitute lipid accumulation in neuroepithelial tumor cells. Features of anaplasia such as nuclear atypia, necrosis and microvascular proliferation are typically absent in primary lesions, but may be found in recurrent tumors with increased mitotic activity, an increased ki-67 proliferation index [3,16,17]. Similarly, the lipidized component may be markedly reduced or even absent in recurrent lesions [17]. Immunohistochemical staining demonstrated both neuronal and glial differentiation. The tumor cells and lipidized cells of liponeurocytoma may express the neuronal markers such as synaptophysin, NSE and microtubule-associated protein 2 (MAP-2). Focal GFAP expression by tumor cells, which indicates astrocytic differentiation, is observed in most cases [18]. Expression of glial markers like GFAP and S-100 are limited to scattered reactive astrocytes [19–21] and a few tumor cells [22–25]. Conveniently, this tumor may have been derived from pluripotential embryonic ectomesenchymal stem cells of neural crest probably persisting in the ventricular matrix and the external granular layer [10,26,27]. Apart from the cerebellar and supratentorial liponeurocytoma, it should be emphasized that the fact about lipidization within the neuroectodermal tumors of the CNS includes cerebellar astrocytomas, multiple intraspinal low-grade astrocytoma, frequently in pleomorphic xanthoastrocytoma, occasionally in glioblastoma, ependymomas and supratentorial PNET [22].

Gross total resection is the golden standard of the treatment. In our case, we also performed gross total resection. Repeat surgery may be preferable to radiotherapy for recurrent liponeurocytoma [3]. But it is unclear whether radiotherapy should be given for recurrent tumor occurred after many years of initial neurosurgery [7,28]. The related reports suggested that the 5-year survival rate of cerebellar liponeurocytoma was 48%, but this should be interpreted with caution because of the paucity of long-term follow-up data [2,11,22]. There are two main surgical approaches for intraventricular neurocytomas including transcortical and transcallosal approaches. Transcallosal approach provides a shorter and more anatomical pathway to the tumor while avoiding the injury to the normal brain cortex. Moreover, transcallosal approach introduces more flexible and direct midline anatomical orientation to the surgeon. Furthermore, some authors reported that the transcallosal approach has better extent of tumor resection and lower incidence of postoperative complications [29].

During transcallosal approach, gene of the internal capsule, which is located lateral to the foramen of Monro should be kept in mind and avoided from injury. Injury to the genu, directly by retraction, might be the reason for transient or permanent hemiparesis, as in our case.

3. Conclusion

Intraventricular liponeurocytoma has distinctive morphologic and immunophenotypic features. It should be kept in mind that liponeurocytomas are not restricted only to the cerebellum, but may infrequently be located in supratentorial intraventricular areas as well. Larger studies based on long-term follow-up are needed in order to clarify clinical features and prognosis of liponeurocytoma.

Conflicts of interest

None of the authors have any conflict of interest, financial or otherwise.

References
